

**REMARKS**

Claims 11-14 and 22-28 are pending in the subject patent application. Claims 11, 12, 23 and 28 have been amended to delete the term "includes" and insert "comprises", as suggested by the examiner. Applicants respectfully note that the term "including" has been given the same meaning in patent claim interpretation as "comprising" (*See, e.g.*, Faber, R.C., *The Mechanics of Patent Claim Drafting*, 3<sup>rd</sup> ed., 1990, p. 11, Practicing Law Institute, New York, *Citing In re Certain Slide Fastener Stringers*, 216 U.S.P.Q. (BNA) 907 (U.S. Int. Tr. Comm. 1981)). Claims 12 (a) and (c) and 27 have been amended to delete the term "a nucleic acid molecule" and insert "the polynucleotide" and claims 12 and 25 also have been amended to delete the term "as set forth in", also as suggested by the examiner. In claims 25, 26 and 28, "nucleic acid molecule" has been deleted and "polynucleotide" inserted, for which antecedent basis is found in claim 12. Claim 14 has been amended to insert "and" between the last two alternative polypeptides so as to recite a proper Markush group. No new matter has been added by this amendment.

Substance of Interview

On December 7, 2005, applicants' representatives, Ms. Petrina Hsi and Dr. Estelle J. Tsevdos discussed with the examiner the support in the originally filed specification for the polypeptide SEQ ID NO:4 including the transmembrane domain, which the specification identifies as spanning amino acids 461-477. (Specification, page 91, lines 12-13). It was noted that all of the polypeptides recited in claim 11 include these amino acids of the transmembrane domain.

Support for the term "**biologically active** polypeptide" in claim 14 was provided in the originally filed specification *inter alia* at page 91, lines 17-18.

The examiner requested that applicants provide a statement providing a nexus between the biological deposit of a plasmid containing cDNA encoding full length beta secretase which has been transformed into *E. coli* cells deposited as ATCC accession no. 207159 and SEQ ID NO:1 which encodes SEQ ID NO:4.

As indicated in applicants' December 7, 2005 Supplemental Amendment, a discrepancy between the U.S. PTO copy of the originally filed specification and applicants' copy of the originally filed specification was discovered during the December 7, 2005 telephone interview. Specifically, the U.S. PTO copy differs by two pages, *i.e.*, is shorter by two pages, than applicants' copy. Therefore, in the U.S. PTO copy of the specification, page 91 corresponds to

applicants' page 93. A comparison of the U.S. PTO copy of the specification with applicant's copy shows that the page margins are shorter starting at page 2, thus moving the text to the following pages. Citations herein to the specification have been revised accordingly to correspond to the pages in the U.S. PTO copy of the specification

Declaration under 37 C.F.R. § 1.132

Applicants submit herewith a Declaration under 37 C.F.R. § 1.132 of Martin Citron, Ph.D., which identifies the deposited *E. coli* as transformed with a plasmid containing cDNA polynucleotide sequence SEQ ID NO:1, which encodes full length beta secretase polypeptide SEQ ID NO:4.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 11, 12, 28 and dependent claims 22-27 have been rejected as indefinite for the recitation of the term "includes", which the examiner suggests replacing with "comprises"; claims 12 and 27 and dependent claims 26 and 28 have been rejected for recitation of "a nucleic acid molecule", which the examiner suggests replacing with "the polynucleotide." Further, claims 12, 25 and dependent claims 26-28 have been rejected for the use of the term "as set forth in".

Although applicants do not agree with this characterization of "including" versus "comprising", the suggested amendments have been made to expedite allowance, and as such, it is believed that the aforementioned amendments obviate the rejections under 35 U.S.C. § 112, second paragraph. Reconsideration and withdrawal of these rejections is respectfully requested.

Rejection under 35 U.S.C. § 112, first paragraph

The examiner has rejected claim 14 as directed to a genus of polypeptides derived from SEQ ID NO:2, which he asserts "have not been disclosed in the specification" and for which "no information, beyond the characterization of SEQ ID NO:2 has been provided by applicants which would indicate that they had possession of the claimed genus of modified polypeptides." The examiner further asserts that "many functionally unrelated polypeptides are encompassed within the scope of these claims."

Applicants respectfully traverse the examiner's rejection and maintain that the examiner has mischaracterized claim 14 as a genus claim. In fact, claim 14 is a Markush claim which

claims three *alternative* isolated biologically active polypeptides: amino acids 45-501; amino acids 46-501; and amino acids 62-501. Applicants respectfully direct the examiner's attention to the specification, as originally filed, at page 24, lines 24 and 29, which specifically identify these amino acids as beta secretase variants. Moreover, each of these polypeptides is biologically active by virtue of the presence of active site domains, amino acids 93-96 and 289-292, as described on page 91 of the specification. (See page 91, lines 17-18) Amino acids 46-501 are described as likely being the "mature, active beta secretase enzyme". (See page 91, lines 18-20) Accordingly, each of the three specifically claimed polypeptides are sufficiently described by the specification as biologically active polypeptides. Further, applicants have amended claim 14 to clarify that the claim recites a proper Markush group by inserting "and" between the last two alternative polypeptides. Therefore, applicants respectfully reconsideration and withdrawal of the rejection of claim 14 under 35 U.S.C. § 112, first paragraph.

Rejection under 35 U.S.C. § 102(e) or 103(a)

The examiner alleges that Gurney *et al.* renders the claimed invention obvious by teaching a polypeptide with SEQ ID NO:4 which is 100% identical to the polypeptide SEQ ID NO:4 of the instant application and a polynucleotide which encodes polypeptide SEQ ID NO:4. Gurney's claimed polypeptide specifically excludes the transmembrane domain as instantly claimed. The examiner maintains that one of skill in the art would have been motivated to make recombinant membrane-bound beta secretase in order to separate the beta secretase protein from all soluble cellular proteins and would have a reasonable expectation of success since Gurney *et al.* provide a polynucleotide sequence encoding the full length polypeptide.

Applicants respectfully traverse the examiner's rejection. The Declaration under 37 C.F.R. § 1.131 of Martin Citron, Ph.D. submitted by applicants on July 22, 2003 has antedated the earliest effective filing date of Gurney *et al.* Therefore, Gurney *et al.* is not 102(e) prior art against applicants' claims. Gurney *et al.* is also not available as prior art under 35 U.S.C. § 103(a). *In re Eickmeyer* clearly states that a declaration under 37 C.F.R. § 1.131 removes the reference as a basis for rejection whether the rejection is based on section 102 or section 103:

The purpose of filing a 131 affidavit (footnote 7 omitted) is to overcome the effective filing date of a reference (footnote 8 omitted) in support of a rejection. **If the 131 affidavit demonstrates that the applicant's date of invention is earlier than the effective date of the reference, the reference is**

**eliminated as support for the rejection.** (n9)<sup>1</sup> *In re Eickmeyer*, 602 F.2d 974, 978 (C.C.P.A. 1979) (Emphasis added)

Accordingly, the Gurney *et al.* patent cannot be relied upon by the Examiner as the basis for any prior art rejections (102 or 103) of the present claims. Applicants respectfully request reconsideration and withdrawal of the rejection.

Potential Interference

Applicants respectfully disagree with the examiner's allegation that a potential interference situation exists between the instant application and Gurney *et al.*

Applicants urge that there is no interference-in-fact since the two-way test<sup>2</sup> under *Eli Lilly & Co. v. Board of Regents of the University of Washington*, 334 F.3d 1264 (Fed. Cir. 2003) is not met. In order for the two-way test to be satisfied, the claimed invention of Gurney *et al.*

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<sup>1</sup> Footnote 9 states: "**this is true whether the rejection is based on section 102 or section 103;** the only difference is that when the rejection is based on section 103, "the purpose of an affidavit is to establish that the claimed invention was made by applicant before the effective date of a reference relied upon to show that the invention was obvious," and "the applicant may prove, by eliminating a reference, that at the time the invention was made, "the subject matter as a whole would (not) have been obvious.'" *Citing In re Tanczyn*, 347 F.2d 830, 832, 52 CCPA 1630, 1632-33, 146 USPQ 298, 300 (1965). (Emphasis added)

*See also In re Zletz:* "Rule 131 (footnote omitted) provides an *ex parte* mechanism whereby a patent applicant may antedate subject matter in a reference, even if the reference describes the same invention that is claimed by the applicant, provided that the same invention is not claimed in the reference when the reference is a United States patent. As explained in (citations omitted), the disclosure in a reference United States patent does not fall under 35 U.S.C. §102(g) but under 35 U.S.C. §102(e), and thus can be antedated in accordance with Rule 131." *In re Zletz*, 893 F.2d 319, 322-323 (Fed. Cir. 1989).

<sup>2</sup> "The critical phrase "assuming invention B is the prior art with respect to invention A" comfortably bears the meaning the Director assigns. Because it is not conclusively known which of the two inventions is the prior art and the critical phrase does not require that invention B is the presumptive senior party, the Director may interpret the phrase to mean that both UW and Lilly may be the assumed "prior art" invention B. Thus, the claimed invention of Party B (UW) is assumed to be prior art vis-a-vis Party A (Lilly) and the claimed invention of Party B (Lilly) is assumed to be prior art vis-a-vis Party A (UW). Thus, under the Director's chosen two-way test, to determine whether two parties are claiming "the same patentable invention," the claimed invention of Party B (UW) must anticipate or render obvious the claimed invention of Party A (Lilly) and the claimed invention of Party B (Lilly) must anticipate or render obvious the claimed invention of Party A (UW). *Eli Lilly & Co. v. Board of Regents of the University of Washington*, 334 F.3d 1264, 1269 (Fed. Cir. 2003).

must anticipate or render obvious the presently claimed invention **and** the presently claimed invention must anticipate or render obvious the claimed invention of Gurney *et al.*

The two-way test is codified in 37 C.F.R. 41.203(a), “interfering subject matter”, *i.e.*, an interference, exists if the **subject matter of a claim** of one party would, if prior art, have anticipated or rendered obvious the **subject matter of a claim** of the opposing party **and vice versa**. (Emphases added).

Gurney *et al.* claim 1 recites:

1. A purified or isolated polypeptide comprising an amino acid sequence that is at least 95% identical to a fragment of the Asp2 protein amino acid sequence of SEQ ID NO:4,

wherein said fragment is a contiguous fragment that includes the aspartyl protease active site tripeptides DTG and DSG and exhibits aspartyl protease activity involved in processing APP into amyloid beta,

**wherein said polypeptide lacks a transmembrane domain,**

and

wherein said polypeptide exhibits aspartyl protease activity in processing APP into amyloid beta. (Emphases added)

The subject matter of Gurney *et al.*’s claim 1 requires that the claimed “**polypeptide lacks a transmembrane domain.**” Applicants’ claimed polypeptide, as recited in presently pending claim 11, comprises the transmembrane (TMD). Accordingly, the subject matter of Gurney’s *et al.*’s claim 1 does not contain each and every element of the subject matter of applicants’ claim 11 and, therefore, cannot anticipate the subject matter of applicants’ claim 1.

Applicants Claim 11, as amended herein, recites:

11. An isolated biologically active beta-secretase polypeptide selected from the group consisting of:

a) the polypeptide of SEQ ID NO: 4;

b) a polypeptide having one to fifty conservative amino acid changes as compared with the polypeptide of SEQ ID NO: 4, wherein **said polypeptide comprises the transmembrane domain;** and

c) the polypeptide encoded by the DNA vector insert of  
ATCC Deposit No. 207159. (Emphases added)

Since the two-way test for "interfering subject matter", *i.e.*, subject matter of a claim of one party (Gurney *et al.*) would, if prior art, have anticipated or rendered obvious the subject matter of a claim of the opposing party (Applicant) **and vice versa**, has not been met, there is no interference-in-fact.

### **CONCLUSION**

In view of the foregoing, it is believed that the subject application is in condition for allowance, a notice of which is earnestly solicited by applicants.

Respectfully submitted,

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*Elizabeth M. Wieckowski*  
Estelle J. Tsevdos  
Registration No. 31,145  
Elizabeth M. Wieckowski  
Registration No. 42,226  
Attorneys for Applicants  
Phone: (212) 309-1021  
Fax: (212) 309-1100